IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

UNITED THERAPEUTICS CORPORATION, Plaintiff, v. LIQUIDIA TECHNOLOGIES, INC., Defendant.	)	C.A. No. 23-975-RGA-SRF

DEFENDANT'S FINDINGS OF FACT RELATED TO NON-INFRINGEMENT OF U.S. PATENT NO. 11,826,327

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TABLE OF ABBREVIATIONS

Asserted Patents & Parties

'327 Patent	U.S. Patent No. 11,826,327
Asserted claims of the '327 patent	Claims 1, 5, 6, 9, 14, 17
UTC/Plaintiff	United Therapeutics Corporation
Liquidia/Defendant	Liquidia Technologies, Inc.

Commonly Used Terms & Abbreviations

6MWD	Six-minute walk distance
DPI	Dry powder inhaler
Dr. Byrd	Dr. Noah Byrd
Dr. Channick	Richard Channick, M.D.
Dr. Nathan	Steven Nathan, M.D.
Dr. Rajeev Saggar	Rajeev Saggar, M.D.
FDA	Food and Drug Administration
FVC	Forced Vital Capacity
FOF	Findings of Fact related to Invalidity of U.S. Patent No. 11,826,327
ILD	Interstitial Lung Disease
INCREASE	A Multicenter, Randomized, Double-Blinded, Placebo-Controlled Trial to Evaluate the Safety and Efficacy of Inhaled Treprostinil in Subjects With Pulmonary Hypertension Due to Parenchymal Lung Disease
iTRE	Inhaled treprostinil
Lancet Publication	S. Nathan, et al., *Inhaled treprostinil and forced vital capacity in patients with interstitial lung disease and associated pulmonary hypertension: a post-hoc analysis of the INCREASE study*, The Lancet Respir. Med, (2021), published online June 29, 2021 https://doi.org/10.1016/S2213-2600(21)00165-X (DTX9)
Mr. Adair	Mr. Jason Adair
PAH	Pulmonary arterial hypertension (Group 1 PH)
PH	Pulmonary hypertension
PH-ILD	Pulmonary hypertension associated with interstitial lung disease (Group 3 PH)
PK	Pharmacokinetics
POSA	Person of ordinary skill in the art
NDA	New Drug Application
NEJM Paper	A. Waxman, et al., *Inhaled Treprostinil in Pulmonary Hypertension Due to Interstitial Lung Disease*, N. Eng. J. Med. 384(4):325 (2021) (DTX363)
NT-proBNP	N-terminal pro b-type natriuretic peptide
UTCFOF	UTC's Proposed Findings of Fact Related to Infringement (D.I. 427)

I. YUTREPIA IS NOT EQUIVALENT TO TYVASO

172. Yutrepia, a dry powder formulation of treprostinil administered by a DPI, was approved to improve exercise ability in PAH and PH-ILD patients in May 2025. Tr. 95:16-18, 173:3-15, 107:16-108:7; PTX291, 4. Liquidia followed the 505(b)(2) pathway and Yutrepia is not a generic of Tyvaso and is a different drug with a different formulation and delivery device from Tyvaso. Tr. 174:6-15, 135:9-25, 53:3-21; PTX377, 2. Use of Yutrepia to improve exercise ability in PAH is not covered by the '327 patent. PTX291, 4; D.I. 96 at 25-26 (citing D.I. 26 at 20).

173. Liquidia's 505(b)(2) NDA cited INCREASE, in addition to its own non-clinical and clinical studies, to support improving exercise capacity in PH-ILD, not to support any approval for the outcomes in claims 5, 6, 9 and 17. PTX377, 3-4; Tr. 214:17-216:25.

174. Because Yutrepia is not a generic drug, it and Tyvaso are not the same "drug product" (they do not have identical dosage forms (dry powder vs. solution)). Dr. Nathan offered no evidence that under the 505(b)(2) pathway, the FDA made a determination that Yutrepia is "pharmaceutically equivalent" or "therapeutically equivalent" to Tyvaso. Nor does Yutrepia have a "Therapeutic Equivalence" ("TE") code from the FDA, such as an AB rating. 21 C.F.R. § 314.3 (Definitions); *see also* https://www.fda.gov/drugs/development-approval-process-drugs/orange-book-preface, §§ 1.2, 1.7 ("A codes," "AB" code) (current as of March 2025); www.fda.gov/media/160054/download.

175. The dosing comparison between Tyvaso and Yutrepia in the Yutrepia label, and the determination of equivalent dosages, was obtained from a PK study in ***healthy*** volunteers and relates to the systemic exposure to treprostinil from a single dose, not local lung delivery or equivalent efficacy between the two drugs. Tr. 192:24-193:13, 159:10-161:8; UTCFOF9, 11, 13.

176. Dr. Rajeev Saggar was asked whether he believes Yutrepia's performance would exceed that of Tyvaso, if used in INCREASE, but not whether "performance" related to safety, efficacy, tolerability, patient satisfaction or some other aspect. Tr. 65:18-24; UTCFOF12.

177. Dr. Nathan relies solely on the INCREASE study for infringement. UTCFOF9-14, 18-21. But Dr. Nathan agreed that INCREASE tested a different drug, Tyvaso, and that if INCREASE were performed with Yutrepia, any prediction as to the results would be "entirely speculat[ive]." Tr. 136:1-137:1, 192:24-193:21, 154:16-156:4. Dr. Nathan also acknowledged that a version of iTRE other than Tyvaso would need to be tested with "their own dataset" to determine if they infringe claims 5, 6, 9 and 17. Tr. 162:16-164:7.

II. YUTREPIA DOES NOT INFRINGE

A. Yutrepia Is Not Indicated for the Outcomes Required by the Claims

178. Yutrepia is only approved to improve exercise ability in PAH and PH-ILD. PTX291, 4; Tr. 173:6-15, 93:22-24. Yutrepia is not approved for a reduction of NT-proBNP; a statistically significant reduction in exacerbations of ILD; a statistically significant improvement in FVC; or an improvement of 10 meters in a 6MWD after 8 weeks of treatment, none of which were primary endpoints in INCREASE. Tr. 175:20-24, 180:10-15, 184:2-4, 189:16-190:13, 146:8-12, 148:8-13, 151:13-18, 153:24-154:10, 116:15-25; PTX147, Table 2. Drs. Byrd, Nathan, Channick, and Mr. Adair agreed that Liquidia is only permitted to promote Yutrepia for its approved indications, which excludes the outcomes recited in claims 5, 6, 9 and 17. Tr. 34:16-35:3, 43:16-44:10, 154:11-15, 176:6-16, 180:10-22, 184:11-21, 175:22-24, 184:2-4, 146:8-11, 148:8-13, 151:13-18, 153:24-154:10; *see also*, UTCFOF7-8. Contrary to UTCFOF11-12, regulations prevent Liquidia from promoting or claiming that Yutrepia performs equivalently to Tyvaso in PAH or PH-ILD, particularly because no head-to-head comparison between the two drugs has been conducted. 21 C.F.R. §§ 202.1(e)(6)(i)-(ii), 201.57(c)(2)(iv).

179. Drs. Channick and Nathan agree that all that is needed to safely and effectively administer Yutrepia is contained in the drug label. Tr. 177:7-17, 194:2-8, 103:3-6.

B. The Claimed Outcomes Are Absent from the Yutrepia Label

180. ***Claim 5.*** Method claim 5 requires a reduction in "plasma concentration of NT-proBNP in the patient by at least 200 pg/ml after 8 weeks, 12 weeks, or 16 weeks of the administering." JTX1, claim 5; Tr. 174:16-20. Claim 5 requires measuring NT-proBNP before and after administration, otherwise a doctor would not know if NT-proBNP levels were reduced. Tr. 174:24-175:12, 205:19-206:19. Both experts agree that the Yutrepia label contains no mention of, or data relating to, NT-proBNP. Tr. 175:25-176:5, 147:14-21. The label does not direct, instruct, or encourage a doctor to seek to achieve the claimed reduction in NT-proBNP in their patient or even measure NT-proBNP. Tr. 176:20-22, 147:14-21, 154:11-15. To safely administer Yutrepia, measuring NT-proBNP is not required. Tr. 176:17-19. And outside of a clinical trial, measuring NT-proBNP is not something that doctors regularly do. Tr. 178:4-16. If a doctor were to measure NT-proBNP, they would be doing so of their own accord. Tr. 177:22-178:2.

181. ***Claim 6.*** Method claim 6 requires a "statistically significant reduction of at least one exacerbation[] of the interstitial lung disease." JTX1, claim 6; Tr. 178:20-180:9. Claim 6 requires a doctor to measure exacerbations before and after administration, otherwise a doctor would not know if exacerbations were reduced. Tr. 179:24-180:2. Both experts agree that the Yutrepia label contains no mention of, or data, statistically significant or otherwise, relating to exacerbations of ILD. Tr. 180:10-15, 180:23-181:5, 148:14-21, 149:20-151:1. The label does not direct, instruct, or encourage a doctor to seek to achieve the claimed reduction in exacerbations in their patient or even measure exacerbations. Tr. 181:11-20. To safely administer Yutrepia, measuring exacerbations of ILD or performing statistical analysis is not required. Tr. 181:21-182:2, 103:3-6.

182. ***Claim 9.*** Method claim 9 requires "a statistically significant improve[ment] of forced vital capacity (FVC) in the patient after 8 weeks, 12, weeks or 16 weeks" of administering inhaled treprostinil. JTX1, claim 9; Tr. 182:14-25. Claim 9 requires a doctor to measure FVC before and after administration, otherwise a doctor would not know if FVC improved. Tr. 183:16-23. Both experts agree that the Yutrepia label contains no mention of, or data, statistically significant or otherwise, relating to FVC. Tr. 184:5-8, 151:19-24. The label does not direct, instruct, or encourage a doctor to seek to achieve the claimed improvement in FVC in their patient or even measure FVC. Tr. 184:22-23, 182:20-25. To safely administer Yutrepia, measuring FVC or performing statistical analysis is not required. Tr. 181:24-182:2, 182:20-25, 194:2-8, 103:3-6.

183. ***Statistically significant***: The "statistically significant" outcomes of claims 6 and 9 require a doctor to treat more than one patient, aggregate the data, and perform a statistical analysis, because statistical significance cannot be determined based on a single patient. Tr. 180:7-9, 118:7-119:1, 799:11-19. The Yutrepia label provides no instruction to treat more than one patient, aggregate data, or perform statistical analysis related to exacerbations or FVC. Tr. 181:11-182:13, 182:20-25, 184:17-185:15. Doctors do not typically perform statistical analysis in clinical practice. Tr. 181:6-10. If a doctor were to measure exacerbations, FVC, or perform statistical analysis, they would be doing so of their own accord. Tr. 185:5-15, 181:6-182:25.

184. ***Claim 17.*** Method claim 17 requires an increase in 6MWD of the patient "by at least 10m after 8 weeks[.]" JTX1, claim 17; Tr. 185:17-20. Claim 17 requires a doctor to measure 6MWD before and after administration, otherwise a doctor would not know if 6MWD improved by at least 10m after 8 weeks. Tr. 186:22-25. There is no requirement that a doctor test 6MWD to determine an improvement in exercise capacity and no instruction in the Yutrepia label to do so. PTX291, § 14.2; Tr. 185:17-195:7. There are numerous other ways to assess exercise capacity,

including patient reporting on activity level, the three-minute step test, cardiopulmonary exercise testing, and functional testing. Tr. 187:12-192:23, 390:23-25, 449:9-16, 471:4-9. The label does not direct, instruct, or encourage a doctor to seek to achieve the claimed 10m increase after 8 weeks in their patient or even measure 6MWD at any time point. To safely use Yutrepia, measuring 6MWD is not required. Tr. 190:7-9. If a doctor were to perform the 6WMD test, they would be doing so of their own accord. Tr. 190:14-21.

C. The Yutrepia Label Does Not Provide Evidence of Infringement

185. Section 14.2 of the Yutrepia label contains only certain results from INCREASE, testing Tyvaso, not Yutrepia. Tr. 192:24-193:21, 154:16-156:4. Section 14.2 contains no mention of NT-proBNP, exacerbations, FVC, or statistical significance of either, and its reference to INCREASE 6MWD does not instruct or require a doctor to measure 6MWD. Tr. 194:13-195:11. Section 14.2 does not allow Liquidia to promote the use of Yutrepia for any of the claimed results. Tr. 194:20-22. Importantly, §6.1 of the label, which Dr. Nathan failed to address, warns doctors against directly comparing results from a clinical trial of one drug with results of a different drug in clinical practice. Tr. 195:17-196:7. Based on this label warning, doctors know not to extrapolate data obtained from one drug with another drug. *Id.*

III. DOCTORS DO NOT NEED TO GO OUTSIDE THE LABEL

186. The experts agree that a drug label must provide doctors with all the information they need to safely prescribe, and that only the label is needed to safely and effectively prescribe. Tr. 177:7-14, 102:18-103:6. Thus, a doctor does not need to review information outside of the Yutrepia label. Tr. 177:4-17, 157:9-14. If a doctor references materials outside the label, they would be doing so of their own accord. Tr. 177:15-17. The Yutrepia label does not instruct doctors to review the INCREASE study publications. Tr. 193:23-194:12.

187. ***NEJM Paper.*** The experts agree that the NEJM Paper, which reports data from the INCREASE study, is not cited in the Yutrepia label. Tr. 196:8-197:7, 156:24-157:1. The Yutrepia label also contains no mention of the Lancet Publication, a post hoc analysis on INCREASE. Tr. 196:8-197:7, 157:3-8. The Yutrepia label does not instruct or encourage a doctor to read these articles nor any other publication or material outside of the label. Tr. 176:23-177:17, 194:2-12.

188. ***Marketing materials.*** UTC contends Liquidia "tells doctors, patients, and payors," that "Yutrepia will achieve results equivalent to Tyvaso in INCREASE." UTCFOF12. None of the documents expressly or implicitly state that Yutrepia is equivalent to Tyvaso, and Liquidia cannot make such a claim. *See* FOF174, 178. Further, neither Dr. Nathan, nor any other witness, testified these documents are final or that they are actually used now that Yutrepia is approved. ***Product Dossier and Formulary Kit*:** UTC cites the Product Dossier and Formulary Kit for their inclusion of NT-proBNP data from INCREASE. UTCFOF18. Both materials are intended for payers, who do not prescribe Yutrepia. PDX3.18; PTX384; PTX385; Tr. 197:12-198:20, 157:25-158:12. The Product Dossier is not in the Yutrepia label and also specifically notes that it "is not to be considered as marketing or promoting the use of Yutrepia." PTX385, 2; Tr. 157:25-158:4, 198:5-11. ***Provider Presentation*:** Dr. Channick was directed to page 41 of the Provider Presentation for reference to INCREASE. PTX391, 41, 65; Tr. 218:8-220:5. But the entire section of the slide deck pertains to "Inhaled treprostinil solution," not Yutrepia. PTX391, 39; Tr. 223:3-224:4. The bottom of each slide is a warning which instructs providers to review the Yutrepia label for full prescribing information. Tr. 224:5-18. ***Other marketing materials*:** Dr. Nathan opined that other marketing materials, falling into 3 "buckets," encourage "all parties" to use Yutrepia, "rely[ing] on the Tyvaso data from the INCREASE study[,]" but Dr. Nathan offered no infringement testimony about any specific pages in these documents. Tr. 109:17-111:8, 127:25-

130:2; UTCFOF12. That is not surprising because they do not mention NT-proBNP, exacerbations of ILD, FVC, or a 10m increase in 6MWD as required by claims 5, 6, 9 and 17. Tr. 198:21-199:23; DDX2.7 (citing PTX348; PTX381; PTX382; PTX383; PTX388; PTX389; and PTX390). PTX386, directed to "specialty distributors," does not mention INCREASE or any claimed endpoint. PTX386. Thus, these documents do not evidence direct or induced infringement.

IV. PK DATA OF INHALED DRUGS DO NOT ESTABLISH INFRINGEMENT

189. Dr. Nathan cited Liquidia's presentation to the J.P. Morgan Healthcare Conference as evidence that Yutrepia will infringe based on "comparable pharmacokinetics." PTX379, 9; Tr. 108:10-109:16; UTCFOF13. PK data, which is systemic blood drug levels, does not reflect efficacy of an inhaled locally-acting drug, like Yutrepia. Tr. 200:1-201:7.

190. The PK data was from a publication titled "Comparative Bioavailability of Inhaled Treprostinil Administered as LIQ 861 and Tyvaso in Healthy Subjects." Tr., 192:24-193:13, 201:8-202:5, 159:10-161:8; UTCFOF13. This PK data was derived from healthy volunteers, not patients with PAH or PH-ILD. Tr. 201:8-202:5, 159:10-161:8. Dr. Channick's unrebutted testimony establishes it is not possible to determine equivalent efficacy based on testing in healthy volunteers. Tr. 201:8-202:5.

191. Dr. Nathan and UTC assert the dependent claims do not require any measurement. UTCFOF6; FOF9-10. But for invalidity, Dr. Nathan testified that to render the claims obvious, a POSA "would need the results of the INCREASE study" because that is what "the[] claims embody." Tr. 865:20-866:5, 843:23-844:14, 849:11-850:23, 851:19-853:4, 856:5-24, 857:16-20. Dr. Nathan and UTC assert, for infringement, the claims require only "one or more" patients to achieve the outcome. Tr. 137:4-10, 119:2-9, 671:15-672:15. But for invalidity, the claims require "virtually all" PH-ILD patients experience an improvement in exercise capacity and the outcomes of the dependent claims. Tr. 925:21-926:4.

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